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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR		ATTORNEY DOCKET NO.
09/377,081	08/19/99	GRASSO	P	19705-001-(A

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EXAMINER	
SAOUD, C	
ART UNIT	**PAPER NUMBER**
1647	12

DATE MAILED: 08/17/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/377,081	GRASSO et al.
Examiner	**Art Unit**
Christine Saoud	1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) [X] Responsive to communication(s) filed on *May 29, 2001*.

2a) [ ] This action is **FINAL**. 2b) [X] This action is non-final.

3) [ ] Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) [X] Claim(s) *1-18, 31-34, 39, and 43-61* is/are pending in the application.

4a) Of the above, claim(s) *5, 43, 44, 46, 47, 49-55, and 57-60* is/are withdrawn from consideration.

5) [ ] Claim(s) _____ is/are allowed.

6) [X] Claim(s) *1-4, 6-18, 31-34, 39, 45, 48, 56, and 61* is/are rejected.

7) [ ] Claim(s) _____ is/are objected to.

8) [ ] Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) [ ] The specification is objected to by the Examiner.

10) [ ] The drawing(s) filed on _____ is/are objected to by the Examiner.

11) [ ] The proposed drawing correction filed on _____ is: a) [ ] approved b) [ ] disapproved.

12) [ ] The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) [ ] Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) [ ] All b) [ ] Some* c) [ ] None of:

1. [ ] Certified copies of the priority documents have been received.
2. [ ] Certified copies of the priority documents have been received in Application No. _____.
3. [ ] Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) [ ] Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) [ ] Notice of References Cited (PTO-892)

16) [ ] Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) [X] Information Disclosure Statement(s) (PTO-1449) Paper No(s). *5, 6*

18) [ ] Interview Summary (PTO-413) Paper No(s). _____

19) [ ] Notice of Informal Patent Application (PTO-152)

20) [ ] Other:

DETAILED ACTION

Response to Amendment

1. Claims 1, 4, 6, 7, 12-13, 18, 31-34, 39 have been amended, claims 19-30, 35-38 and 40-42 have been canceled and claims 43-61 have been added as requested in the amendment of paper #9, filed 20 February 2001. Claims 1-18, 31-34, 39, and 43-61 are pending in the instant application.

Election/Restriction

2. Applicant's election without traverse of Group I in Paper No. 9 is acknowledged. Applicant's election of the species encompassed by SEQ ID NO:18 in Paper No. 11 is acknowledged. Claims 5, 43-44, 46-47, 49-55, and 57-60 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 11.

Drawings

3. Figures 2, 3, 4, 6, 10, 11, and 13 of the instant application is represented by separate panels and/or pages. 37 C.F.R. § 1.84(u)(1) states that when partial views of a drawing which are intended to form one complete view, whether contained on one or several sheets, must be identified by **the same number followed by a capital letter**. For example, the 7 pages of drawings which are labeled "FIG. 4" and "FIG.4 (con't)" in the instant specification should be renumbered Figures "4A" through "4N". Applicant is reminded that once the drawings are

changed to meet the separate numbering requirement of 37 C.F.R. § 1.84(u)(1), the Brief Description of the Drawings and the rest of the specification should be amended accordingly to reflect this separate numbering requirement. For example, the reference to Figure 4 at page 11, line 25 is incorrect and should be "Figure 4A-4N". Correction of either the Figures, the reference to the Figures in the specification, or both is required as outlined above.

Specification

4. The disclosure is objected to because of the following informalities: at page 48, line 7, the identified amino acid sequence must be represented by a Sequence Identifier (see 37 CFR 1.821(d)).

Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-3, 7, 8-18, 31-34, and 39 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims encompass "homologs, analogs and derivatives" of a purified leptin peptide. The instant specification indicates that these terms are directed to species homologs (page 20), variants differ from the polypeptide of the present invention "but retaining essential properties thereof" (page 20), peptides which are related to animals, insects, plants, or human leptin (page 21), and that such can be isolated (see page 21) using hybridization techniques. However, the instant specification fails to provide an adequate written description of such "homologs, analogs or derivatives" such to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is because homologs are usually naturally occurring molecules which have a defined structure which cannot be predicted based on the structure provided in the instant specification. For example, although one of ordinary skill in the art would reasonably expect a given protein to have various allelic forms or have various alternative amino acid substitutions (usually one to three) depending on the source of the protein, one cannot predict what these substitutions will be, therefore, there is not a written description of such. As the instant claims are directed to subject matter which has yet to be described or isolated, the instant specification lacks a written description of this subject matter, absent evidence to the contrary.

7. Claims 1-4, 6-18, 31-34, 39, 45, 48, 56 and 61 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a leptin fragment comprising the amino acid sequence of SEQ ID NO:2 or 18 (murine and human, respectively), does not reasonably provide enablement for a leptin peptide lacking these amino acid sequences, such as % homology, amino acid substitutions, derivatives, etc. as recited in the claims. The specification

does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. .

The specification teaches that several fragments of leptin have modulatory activity on body mass. The specification specifically exemplifies the peptide of SEQ ID NO:18, which is the elected species. The claims are directed to leptin peptides, fragments, homologs, analogs, and derivatives, encompass % homology, amino acid substitutions and variant forms of leptin. However, the instant specification only provides for naturally occurring peptides of leptin which have modulatory activity on body mass and fails to describe a single peptide with a non-naturally occurring amino acid sequence which modulates body mass. The instant specification provides a number of methods and assays for making and testing for molecules which could be made, but this would require undue experimentation for one of ordinary skill in the art to determine which proteins which meet the structural limitations of the claims would also meet the functional limitations in light of the lack of guidance as to which amino acids could be modified and still obtain a leptin peptide with the recited activity. The instant specification lacks the appropriate guidance to alter the disclosed peptides (in light of the fact that no alterations have been made) and obtain one with the required activity. The specification is only enabling for leptin peptides having a naturally occurring amino acid sequence (such as SEQ ID NO:2 or 18) because it does not describe the production of any leptin peptide ***lacking*** that sequence.

In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970), held that

> "Inventor should be allowed to dominate future patentable inventions of others where those inventions were based in some way on his teachings, since such improvements while unobvious from his teachings, are still within his contribution,

> since improvement was made possible by his work; however, he must not be permitted to achieve this dominance by claims which are insufficiently supported and, hence, not in compliance with first paragraph of 35 U.S.C. 112; that paragraph requires that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific law; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved."

By following the guidance presented in the instant specification and sound scientific principles, a practitioner can **not** produce a leptin peptide lacking the disclosed amino acid sequence and predict the functional properties of that protein.

Additionally, the pending claims encompass non-naturally occurring mutants of leptin having the disclosed amino acid sequences but does not explicitly identify those amino acid residues which are critical for the biological activity of modulating body mass. In the absence of guidance, a practitioner of the art of molecular biology would have to resort to a substantial amount of experimental trial and error in the form of deletional and substitutional analysis to identify those critical residues as would be needed to produce a mutant of the disclosed peptide. This trial and error would clearly constitute undue experimentation and, therefore, the instant specification is not enabling for the production of such mutants, which are clearly claimed. The standard for an enabling disclosure is not one of making and testing and the claims constitute a "wish to know". In so far as the instant claims encompass a leptin peptide having a sequence

other than the disclosed sequences identified above, specific case law bears on this issue: Amgen Inc. v. Chugai Pharmaceuticals Co. Ltd., 18 U.S.P.Q. 2d, 1016, held that;

> "A gene is a chemical compound, albeit a complex one, and it is well established in our law that conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials, and describe how to obtain it. *See Oka*, 849 F.2d at 583, 7 USPQ2d at 1171. Conception does not occur unless one has a mental picture of the structure of the chemical, or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by its principal biological property, *e.g.*, encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property. We hold that when an inventor is unable to envision the detailed constitution of a gene so as to distinguish it from other materials, as well as a method for obtaining it, conception has not been achieved until reduction to practice has occurred, *i.e.*, until after the gene has been isolated."

The fact pattern is directly analogous in that what is claimed are proteins that have yet to be isolated or characterized for the activity recited in the application and thereby constitutes a "wish to know" rather than a reduction to practice, absent evidence to the contrary. *In re Clarke*, 148 USPQ 665, (CCPA 1966) held that;

> It appears to be well settled that a single species can rarely, if ever, afford sufficient support for a generic claim. In re Soll, 25 C.C.P.A. (Patents) 1309, 97 F.2d 623, 38 USPQ 189 ; In re Wahlforss et al., 28 C.C.P.A. (Patents) 867, 117 F.21 270, 48 USPQ 397 . The decisions do not however fix any definite number of species which will establish completion of a generic invention and it seems evident therefrom that such number will vary, depending on the circumstances of particular cases. Thus, in the case of a small genus such as the halogens, consisting of four species, a reduction to practice of three, or perhaps even two, might serve to complete the generic invention, while in the case of a genus comprising hundreds of species, a considerably large number of reductions to practice would probably be necessary.

Therefore, the claims are not enabled for their full breadth as outlined above.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 4, 6, 8-12, 18, 31, 32, 33, 45, 48, 56, 61, xx are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 4 and 6 contain the recitation of "may be", which is indefinite because it is not clear if these are the only items that these elements "may be" or if these elements "may be" other things as well. For example, claim 4 attempts to define elements "Xaa_n" and "Xaa_1, Xaa_2, and Xaa_3" by what they "may be". This recitation is indefinite because while these elements "may be" what is recited, it also allows for them to be other things which are not defined. It is not clear if the claim intends these elements to be anything (as implied by the recitation that they "may be" a particular thing), or if they are only to be those elements which are recited in the claims. Clarification is necessary to determine the metes and bounds of the claims.

Claims 8-11 and 45 are unclear and indefinite for reciting "mammalian", "murine", "human", and "synthetic" in that it is not clear these peptides are to be distinguished one from another when the only physical limitations present are amino acid sequence. In other words, what would make a peptide "human" rather than "synthetic" if they both have the same amino acid sequence? Wouldn't a synthetic peptide which has a human amino acid sequence be a human peptide? Or if a peptide which has an amino acid sequence which is common to both the murine and human peptides, it is human or murine? Applicant may wish to clarify these claims as product

by process claims, since the recitation of "mammalian", "murine", "human", and "synthetic" fail to convey any distinguishing limitations for the reasons provided above.

Claims 12 and 61 are unclear and indefinite for reciting a peptide comprising amino acids (or amino acid residues). These claims are confusing because it is not clear if the peptide has a specific amino acid sequence, or if the peptide just comprises the amino acids in the recited sequence in any given order. The claims are being interpreted as comprising the amino acid "sequence", and if this is the correct interpretation, the claims should be amended to recite such.

Claims 18, 31, 32, and 33 are unclear and confusing for reference to "any one of the peptides of claim 1" (or similar language). Claim 1 is limited to a single peptide, therefore, reference to "any one of" in the dependent claims is not consistent with the language of claim 1. Correction is required.

Claim 45 is unclear and indefinite for depending from a non-elected claim. It would appear, upon reviewing claim 43, that this claim does not read on the elected species in that Applicant did not indicate that claim 43 reads on the elected species. Applicant may wish to clarify which claims read on the elected species in the next Office action.

Claim 48 is unclear and indefinite for depending from a non-elected claim. It would appear, upon reviewing claim 43, that this claim does not read on the elected species in that Applicant did not indicate that claim 43 reads on the elected species. Applicant may wish to clarify which claims read on the elected species in the next Office action.

Claim 56 is unclear and indefinite for depending from a non-elected claim. It would appear, upon reviewing claim 50, that this claim does not read on the elected species in that

Applicant did not indicate that claim 50 reads on the elected species. Applicant may wish to clarify which claims read on the elected species in the next Office action.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

11. Claims 1-4, 6-18, 39, 45, and 61 are rejected under 35 U.S.C. 102(a/b) as being anticipated by Grasso et al. (Endocrinol. 138:1413-1418, 1997).

It is noted that the instant application has priority to August 1998. It is not clear which month the instant reference was published, therefore, it is either an (a) or (b) reference. As the Applicant is one of the co-authors of the reference, Applicant may wish to clarify the publication date of the reference. Accordingly, the rejection is being made under both 102(a) and (b) in the alternative in the event that the publication date is before or after August 21, 1997.

Grasso et al. teach various leptin fragments which meet the limitations of the instant claims (see Table 1, page 1414). Grasso et al. do not specifically teach a kit comprising the leptin fragments, however, as the leptin peptides were synthesized and purified by HPLC, they would have had to been stored at some point, thereby being in a container and meeting the limitations of

this claim (claim 39). Some of the instant claims are directed to peptides which are human, however, as the structure of the peptide is dependent from the amino acid sequence and the amino acid sequence is comprised in the mouse peptide (see SEQ ID NO:18), it would appear that the peptides would be indistinguishable and not materially different from the murine protein of the prior art. The recitation that the protein be of human origin is essentially defining the product by the process of making it. The decisional law has clearly emphasized that product-by-process claims are directed to a product and not restrictive to a process because they are not construed as being limited to a product of a specific process (In re Bridgeford, 149 USPQ 55; In re Hirao, 190 USPQ 15). Patentability depends on whether the product is known in the art or obvious and is not governed by its process of production (In re Klug, 142, USPQ 161); therefore, the burden is upon Applicants to establish a patentable difference (In re Fessman, 180 USPQ 324). Further held was that when a prior art product reasonably appears to be the same as the claimed, but differs by the process in which it was produced, a rejection of this nature is eminently fair and the burden is upon appellants to prove, by comparative evidence, a patentable difference (In re Brown, 173 USPQ 685; In re Marosi, 218 USPQ 289; In re Thorpe, 227 USPQ 965; In re Fitzgerald, 205 USPQ 594; and as more recently emphasized in Ex parte Gray, 10 USPQ 2d 1922; Amgen Inc. v. Chugai Pharmaceutical Co., 9 USPQ 2d 1833; and Scripps Clinic v. Genetech Inc., 3 USPQ 2d 1481). In the instant situation, there does not appear to be a distinguishable difference from the murine leptin protein comprising the amino acid sequence of SEQ ID NO:18 of the prior art and the human leptin peptide of the instant claims, therefore the instant claims are anticipated by the prior art.

12. Claims 1, 2, 3, 9, 10, 11, 12, 13, 14, 16, 18, 33, 39 are rejected under 35 U.S.C. 102(b) as being anticipated by Samson et al. (Endocrinol. 137(11): 5182-5185, 1996).

Samson et al. teach a leptin peptide of 35 amino acids which modulates body mass, thereby, anticipating the instant claims.

13. Claims 1-4, 6-18, 39, 61 are rejected under 35 U.S.C. 102(a) as being anticipated by Al-Barazanji et al. (WO 97/46585, 12/11/1997).

Al-Barazanji et al. teach leptin peptides, including a peptide which comprises the amino acid sequence of SEQ ID NO:18 (see page 1, lines 35-39), wherein the peptides modulate body mass, thereby, anticipating the instant claims.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christine J. Saoud, Ph.D., whose telephone number is (703) 305-7519. The examiner can normally be reached on Monday to Friday from 7AM to 3PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 308-4556. If this number is out of service, please call the Group receptionist for an alternate number. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. Official papers should NOT be faxed to 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

August 14, 2001

CHRISTINE J. SAOUD
PRIMARY EXAMINER

Christine J. Saoud